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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.

EXAMINER	
ART UNIT	PAPER NUMBER
	12

DATE MAILED:

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No.	Applicant(s)	
	09/492,361	JENTSCH, THOMAS J	
	Examiner	Art Unit	
	Joseph F Murphy	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-45,47 and 49-58* is/are pending in the application.

4a) Of the above claim(s) *12-17,31-45,47 and 49-58* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11 and 18-30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s) _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group I, claims 1-11 and 18-30 in Paper No. 10, 6/13/2001 is acknowledged. The traversal is on the ground(s) that i) there is no undue burden to search the entire application and ii) the sequences are not distinct. This is not found persuasive for the following reasons.

Applicant's attention is directed to MPEP 808.02 which states that "Where the related inventions as claimed are shown to be distinct under the criteria of MPEP 806.05 (c-i), the examiner, in order to establish reasons for insisting upon restriction, must show by appropriate explanation one of the following: (A) Separate classification thereof; (B) A separate status in the art when they are classifiable together; (C) A different field of search." As set forth in the Restriction requirement, the separate classification established for each Group demonstrates that each distinct Group has attained recognition in the art as a separate subject for inventive effort, and also a separate field of search. Thus, the Restriction requirement is proper.

Applicant argues that no burden is placed on the examiner to consider all claims. As discussed in above, the separate classification established for each Group demonstrates that each distinct Group requires a separate field of search, and a search of one Group would not reveal art on the other Groups, thus imposing a burden on the examiner.

The requirement is still deemed proper and is therefore made FINAL. Claims 12-17,31-45,47 and 49-58 are withdrawn from further consideration pursuant to 37 CFR 1.142(b).

Specification

The title of the invention is not descriptive. Applicant should avoid the use of novel in the title, as patents are presumed to be novel and unobvious.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 18-27 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. The claims read on an organism, i.e. a human being, comprising the transfected cell.

Claim Rejections - 35 USC § 112 first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 2, 9, 10, 11, 20, 21, 22 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated polynucleotide having a sequence as set forth in SEQ ID NO: 1, does not reasonably provide enablement for an isolated polynucleotide wherein the polynucleotide is at least 50, 70, 80, 90, 95% homologous to the nucleotide sequence set forth in SEQ ID NO: 1. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claims 2, 9, 10, 11, 20, 21, 22 are overly broad in the recitation of "is at least 50, 70, 80, 90, 95% identical" since no guidance is provided as to which of the myriad of variant or mutated polypeptide species encoded by the polynucleotides which are encompassed by the limitations of the claims will retain the characteristics of a KCNQ4 potassium channel. In the specification (page 5, lines 10), Applicants disclose that the mutated polynucleotide may be a polynucleotide

of the invention having a nucleotide sequence encoding a potassium channel having an amino acid sequence that has been changed at one or more positions, without disclosing any actual or prophetic examples on expected performance parameters of any of the possible variants or muteins of the KCNQ4 potassium channel. However, it is known in the art that even single amino acid changes or differences in the amino acid sequence of a protein can have dramatic effects on the protein's function. For example, Mikayama et al. (1993) teaches that the human glycosylation-inhibiting factor (GIF) protein differs from human migration inhibitory factor (MIF) by a single amino acid residue (page 10056, Figure 1). Yet, despite the fact that these proteins are 90% identical at the amino acid level, GIF is unable to carry out the function of MIF, and MIF does not exhibit GIF bioactivity (page 10059, second column, third paragraph). It is also known in the art that a single amino acid change in a protein's sequence can drastically affect the structure of the protein and the architecture of an entire cell. Voet et al. (1990) teaches that a single Glu to Val substitution in the beta subunit of hemoglobin causes the hemoglobin molecules to associate with one another in such a manner that, in homozygous individuals, erythrocytes are altered from their normal discoid shape and assume the sickle shape characteristic of sickle-cell anemia, causing hemolytic anemia and blood flow blockages (pages 126-128, section 6-3A and page 230, column 2, first paragraph).

There is no guidance provided in the specification as to how one of ordinary skill in the art would generate a nucleic acid sequence encoding a KCNQ4 potassium channel other than those exemplified in the specification. See In re Wands, 858 F.2d at 737, 8 USPQ2d at 1404. The test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue. The factors to be considered when determining

whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue" include, but are not limited to: (1) the breadth of the claims; (2) the nature of the invention; (3) the state of the prior art; (4) the level of one of ordinary skill; (5) the level of predictability in the art; (6) the amount of direction provided by the inventor; (7) the existence of working examples; and (8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure. Given the breadth of claims 2, 9, 10, 11, 20, 21, 22 in light of the predictability of the art as determined by the number of working examples, the level of skill of the artisan, and the guidance provided in the instant specification and the prior art of record, it would require undue experimentation for one of ordinary skill in the art to make and use the claimed invention.

Claims 2, 9, 10, 11, 20, 21, 22 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

These are genus claims. In the specification (page 5, lines 10), Applicants disclose that the mutated polynucleotide may be a polynucleotide of the invention having a nucleotide sequence

encoding a potassium channel having an amino acid sequence that has been changed at one or more positions. The specification and claims do not indicate what distinguishing attributes shared by the members of the genus. Thus, the scope of the claim includes numerous structural variants, and the genus is highly variant because a significant number of structural differences between genus members is permitted. Although the specification states that these types of changes are routinely done in the art, the specification and claim do not provide any guidance as to what changes should be made. Structural features that could distinguish compounds in the genus from others in the protein class are missing from the disclosure. No common structural attributes identify the members of the genus. The general knowledge and level of skill in the art do not supplement the omitted description because specific, not general, guidance is what is needed. Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variant, SEQ ID NO: 1 alone is insufficient to describe the genus. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, applicant was not in possession of the claimed genus.

Claims 18-27 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a host cell in culture comprising a polynucleotide with the sequence as set forth in SEQ ID NO: 1, does not reasonably provide enablement for in vivo transfection. The

specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The specification on page 16, lines 1-17 discloses that the nucleic acids of the current invention can be expressed in a wide variety of host cell types, including cells within a host animal. However, there are no actual or prophetic examples that disclose how to make or use host cells that comprise a DNA sequence as set forth in SEQ ID NO: 1 in an animal. The Examiner cites Eck & Wilson (page 81, column 2, second paragraph to page 82, column 1, second paragraph) who report that numerous factors complicate *in vivo* gene expression which have not been shown to be overcome by routine experimentation. These include, the fate of the DNA vector itself (volume distribution, rate of clearance into the tissues, etc.), the *in vivo* consequences of altered gene expression and protein function, the fraction of vector taken up by the target cell population, the trafficking of the genetic material within cellular organelles, the rate of degradation of the DNA, the level of mRNA produced, the stability of the mRNA produced, the amount and stability of the protein produced, and the protein's compartmentalization within the cell, or its secretory fate, once produced. Since the instant disclosure does not address any of the methods necessary to make a host cell in an animal which comprises the polynucleotide of interest, therefore, the claims as written are not enabled.

The instant disclosure does not address any of the methods necessary to make a host cell in an animal which comprises the polynucleotide of interest, therefore, the claims as written are not enabled. Addition of the limitation "isolated cell" to the claims would obviate this rejection.

Claim Rejections - 35 USC § 112 second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-11, 18-30 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 recites the term "high stringency conditions", which is a conditional term and renders the claim indefinite. Furthermore, some nucleic acids which might hybridize under conditions of moderate stringency, for example, would fail to hybridize under conditions of high stringency. The metes and bounds of the claim thus cannot be ascertained. This rejection could be obviated by supplying specific conditions supported by the specification which Applicant considers to be "high stringency". Claims 2-11, 18-30 are rejected insofar as they depend on the recitation in claim 1 of "high stringency conditions".

The recitation of the term "sub sequence" renders claims 5-6 indefinite. There is no guidance provided as to what specific sequences the term "sub-sequence" refers to. Therefore, the metes and bounds of the claim are unclear

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 3-11 and 18-30 are rejected under 35 U.S.C. 102(b) as being anticipated by Singh et al. (1998).

Singh et al. discloses the nucleotide and amino acid sequence of a potassium channel, KCNQ2, cloned from a fetal brain cDNA library (page 27, Figure 3). The nucleic acid taught in Singh et al. would hybridize under high stringency conditions to the nucleotide sequence SEQ ID NO: 1 of the instant application, thus anticipating claim 1 (see Sequence Comparison A, attached). The nucleic acid of Singh et al. was cloned from a cDNA library, thus anticipating claims 3-4, and comprises a sub-sequence of SEQ ID NO: 1, thus claims 5-6 are anticipated. The nucleic acid of Singh et al. encodes a potassium channel, and can be considered a variant of SEQ ID NO: 1, thus claims 7-9 are anticipated. The nucleic acid of Singh et al. was subcloned, thus anticipating claims 18-27. Table I comprises the sequence of KCNQ2, thus the limitations of claims 10-11 are met.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 3-11 and 18-30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Singh et al. (1998) in view of WO 9401548 (Sibson et. al.).

The teaching of Singh et al. has been set forth, above. Singh et al. does not teach methods of producing a protein.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the invention of Sibson et al. by substituting a cDNA in the polycloning region of the vector with the polynucleotide (cDNA) of Singh et al. for the purpose of transfecting a host cell as taught by Sibson et al. in view of Sibson et al.'s suggestion that it would be desirable to do so (pages 8-13). One of ordinary skill in the art would have been motivated to make this substitution in order to express the protein encoded by the introduced DNA in a host cell to perform ligand binding and functional assays. There would have been a reasonable expectation of success for a person of ordinary skill in the art to make this invention since these techniques are widely used in the art and are highly successful (Sibson et al., page 10, line 38 - page 12, line 42). The present invention, therefore, is *prima facia* obvious over the above references in the absence of evidence to the contrary.

Conclusion

No claim is allowed.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph F. Murphy whose telephone number is 703-305-7245. The examiner can normally be reached on M-F 7:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached on 703-308-6564. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-308-0294 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Joseph F. Murphy, Ph. D.
Patent Examiner
Art Unit 1646
August 16, 2001

Prema Mertz
PREMA MERTZ
PRIMARY EXAMINER